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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,419	08/14/1998	DOUGLAS T. ROSS	23138-S	7968
29728 7590 10/31/2007 GUILFORD PHARMACEUTICALS C/O FOLEY & LARDNER LLP 3000 K STREET, NW WASHINGTON, DC 20007-5143			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 10/31/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Response to Rule 312 Communication</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/134,419	ROSS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Patrick T. Lewis	1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

1. ☒ The amendment filed on 25 October 2007 under 37 CFR 1.312 has been considered, and has been:

a) ☐ entered.

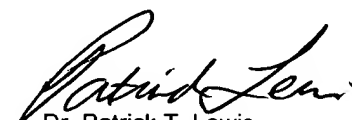
b) ☒ entered as directed to matters of form not affecting the scope of the invention.

c) ☐ disapproved because the amendment was filed after the payment of the issue fee.

Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

d) ☐ disapproved. See explanation below.

e) ☐ entered in part. See explanation below.

  
 Dr. Patrick T. Lewis  
 Primary Examiner  
 Art Unit: 1623



**FOLEY & LARDNER LLP**  
**ATTORNEYS AT LAW**  
 WASHINGTON HARBOUR  
 3000 K STREET NW, SUITE 500  
 WASHINGTON, D.C. 20007-5143  
 TELEPHONE: 202.672.5300  
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## FACSIMILE TRANSMISSION

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**Total # of Pages : 16 (including this page)**

TO:	PHONE #:	FAX #:
<b>Examiner Patrick T. Lewis</b> <b>U.S. Patent and Trademark Office</b>	<b>(571) 272-0655</b>	<b>(571) 273-0655</b>

**From : Rouget F. Henschel**

**Date : October 25, 2007**

**Client/Matter No : 087579-0857**

**User ID No : 3740**

### MESSAGE:

Re: U.S. Patent Application No. 09/134,419

Dear Examiner Lewis:

We have filed the attached in response to the two Notices to File Corrected Application Papers dated July 24, 2007. Please contact me if you have any questions at (202) 295-4059.

If there are any problems with this transmission or if you have not received all of the pages, please call .

Operator:	Time Sent:	Return Original To: <b>Kevin Mallett's desk</b>
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**CONFIDENTIALITY NOTICE: THE INFORMATION CONTAINED IN THIS FACSIMILE MESSAGE IS INTENDED ONLY FOR THE PERSONAL AND CONFIDENTIAL USE OF THE DESIGNATED RECIPIENTS NAMED ABOVE. THIS MESSAGE MAY BE AN ATTORNEY-CLIENT COMMUNICATION, AND AS SUCH IS PRIVILEGED AND CONFIDENTIAL. IF THE READER OF THIS MESSAGE IS NOT THE INTENDED RECIPIENT OR ANY AGENT RESPONSIBLE FOR DELIVERING IT TO THE INTENDED RECIPIENT, YOU ARE HEREBY NOTIFIED THAT YOU HAVE RECEIVED THIS DOCUMENT IN ERROR, AND THAT ANY REVIEW, DISSEMINATION, DISTRIBUTION OR COPYING OF THIS MESSAGE IS STRICTLY PROHIBITED. IF YOU HAVE RECEIVED THIS COMMUNICATION IN ERROR, PLEASE NOTIFY US IMMEDIATELY BY TELEPHONE AND RETURN THE ORIGINAL MESSAGE TO US BY MAIL. THANK YOU.**

Atty. Dkt. No. 087579-0857

***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***

Title: CARBOXYLIC ACIDS AND  
ISOSTERES OF N-  
HETEROCYCLIC  
COMPOUNDS FOR VISION  
AND MEMORY DISORDERS

Appl. No.: 09/134,419

Filing Date: 8/14/1998

Examiner: Patrick T. LEWIS

Art Unit: 1623

Confirmation 7968  
Number:

**AMENDMENT TRANSMITTAL**

Mail Stop Issue Fee  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Transmitted herewith is an Amendment and Transmittal of Replacement Pages and Additional Formal Drawings, in the above-identified application.

[ ] Small Entity status under 37 C.F.R. § 1.9 and § 1.27 has been established by a previous assertion of Small Entity status.

[ ] Assertion of Small Entity status is enclosed.

Atty. Dkt. No. 087579-0857

☐ The fee required for additional claims is calculated below:

	Claims As Amended		Previously Paid For		Extra Claims Present		Rate		Additional Claims Fee
Total Claims:	3	-	26	=	0	x	\$50.00	=	\$0.00
Independent Claims:	1	-	3	=	0	x	\$210.00	=	\$0.00
First presentation of any Multiple Dependent Claims:						+	\$370.00	=	\$0.00
CLAIMS FEE TOTAL									\$0.00

☐ Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

<input type="checkbox"/> Extension for response filed within the first month:	\$120.00	\$0.00
<input type="checkbox"/> Extension for response filed within the second month:	\$460.00	\$0.00
<input type="checkbox"/> Extension for response filed within the third month:	\$1,050.00	\$0.00
<input type="checkbox"/> Extension for response filed within the fourth month:	\$1,640.00	\$0.00
<input type="checkbox"/> Extension for response filed within the fifth month:	\$2,230.00	\$0.00
EXTENSION FEE TOTAL:		\$0.00
<input type="checkbox"/> Statutory Disclaimer Fee under 37 C.F.R. 1.20(d):	\$130.00	\$0.00
CLAIMS, EXTENSION AND DISCLAIMER FEE TOTAL:		\$0.00
<input type="checkbox"/> Small Entity Fees Apply (subtract ½ of above):		\$0.00
Extension Fees Previously Paid:		\$0.00
TOTAL FEE:		\$0.00

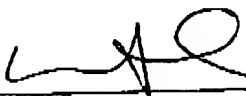
If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Atty. Dkt. No. 087579-0857

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date 25-OCT-2007

By 

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 295-4059  
Facsimile: (202) 672-5399

Rouget F. Henschel  
Attorney for Applicant  
Registration No. 39,221



## UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
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Application No. : 09/134,419  
Applicant : Ross et al.  
Filing Date : 8/14/98  
Date Mailed : 7/24/07

**NOTICE TO FILE CORRECTED APPLICATION PAPERS*****Notice of Allowance Mailed***

This application has been accorded an Allowance Date and is being prepared for issuance. The application, however, is incomplete for the reasons below.

Applicant is given 30 days from the mail date of this Notice within which to correct the informalities indicated below. If the informality pertains to the abstract, specification (including claims) or drawings, the informality must be corrected with an amendment in compliance with 37 CFR 1.121 (or, if the application is a reissue application, 37 CFR 1.173). Such an amendment may be filed after payment of the issue fee if limited to correction of informalities noted herein. See Waiver of 37 CFR 1.312 for Documents Required by the Office of Patent Publication, 1280 Off. Gaz. Patent Office 918 (March 23, 2004). In addition, if the informality is not corrected until after payment of the issue fee, for purposes of 35 U.S.C. 154(b)(1)(iv), "all outstanding requirements" will be considered to have been satisfied when the informality has been corrected. A failure to reply will result in the application being ABANDONED. This period for reply is NOT extendable under 37 CFR 1.136(a).

Some of the information on pages 18, 38, 39 and 74 of the specification is illegible. Applicant must submit legible copies of the specification's pages 18, 38, 39 and 74.

*A copy of this notice **MUST** be returned with the reply. Please address response to "Mail Stop Issue Fee, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450".*

A handwritten signature in black ink, appearing to read "Dale G. Olson".

Dale G. Olson  
Office of Patent Publication  
Phone: 703-308-9250 ext. 122



## UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
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Application Number : 09/134,419

Applicant : Ross et al.

Filing Date : 8/14/98

Date Mailed : 7/24/07

**NOTICE TO FILE CORRECTED APPLICATION PAPERS*****Notice of Allowance Mailed***

This application has been accorded an Allowance Date and is being prepared for issuance. The application, however, is incomplete for the reasons below.

Applicant is given 60 days from the mail date of this Notice within which to correct the informalities indicated below. If the informality pertains to the abstract, specification (including claims) or drawings, the informality must be corrected with an amendment in compliance with 37 CFR 1.121 (or, if the application is a reissue application, 37 CFR 1.173). Such an amendment may be filed after payment of the issue fee if limited to correction of informalities noted herein. See Waiver of 37 CFR 1.312 for Documents Required by the Office of Patent Publication, 1280 Off. Gaz. Patent Office 918 (March 23, 2004). In addition, if the informality is not corrected until after payment of the issue fee, for purposes of 35 U.S.C. 154(b)(1)(iv), "all outstanding requirements" will be considered to have been satisfied when the informality has been corrected. A failure to reply will result in the application being ABANDONED. This period for reply is NOT extendable under 37 CFR 1.136(a).

The illustrations on pages 65, 67 and 68 of the specification do not come within the exceptions of 37 CFR 1.58 (a). Please delete the illustrations from the specification, provide the illustrations as part of the formal drawings in accordance with 37 CFR 1.84, and amend the specification, as necessary, in accordance with 37 CFR 1.74.

*A copy of this notice **MUST** be returned with the reply. Please address response to "Mail Stop Issue Fee, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450".*

A handwritten signature in black ink, appearing to read "Dale G. Olson".

Dale G. Olson  
Office of Patent Publication  
Phone: 703-308-9250 ext. 122



Atty. Dkt. No. 087579-0857

***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***

Title: CARBOXYLIC ACIDS AND ISOSTERES OF  
N-HETEROCYCLIC COMPOUNDS FOR  
VISION AND MEMORY DISORDERS

Appl. No.: 09/134,419

Filing Date: 08/14/1998

Examiner: Patrick T. LEWIS

Art Unit: 1623

Confirmation 7968  
Number:

**AMENDMENT AND TRANSMITTAL OF REPLACEMENT PAGES  
AND ADDITIONAL FORMAL DRAWINGS**

Mail Stop Issue Fee  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Applicants attach two Notices to File Corrected Application Papers, both mailed July 24, 2007.

Responsive to the first Notice to File Corrected Application Papers mailed July 24, 2007, Applicants submit the attached replacement pages 18, 38-39, and 74 of the specification.

Responsive to the second Notice to File Corrected Application Papers dated July 24, 2007, Applicants submit the formal drawings (3 sheets, showing Figs. 10-12), corresponding to Tables V, VI, and VII, and Applicants delete Tables V, VI, and VIII from the specification, as requested in the second Notice.

**Amendments to the Specification** begin on page 2 of this document.

**Remarks/Arguments** begin on page 3 of this document.

Please amend the application as follows:

Atty. Dkt. No. 087579-0857

**Amendments to the Specification:**

Please amend the specification as follows:

Please delete the illustration and all paragraphs on page 65, including the text "TABLE V".

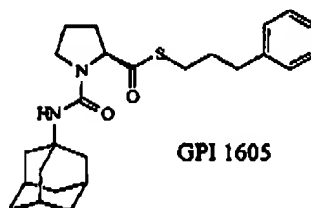
Please delete the illustration and all paragraphs on page 67, including the text "TABLE VI".

Please delete the illustration and all paragraphs on page 68, including the text "TABLE ,VII".

**DETAILED DESCRIPTION OF THE INVENTION****Definitions**

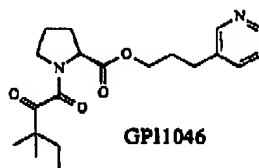
"Eye" refers to the anatomical structure responsible for vision in humans and other animals, and encompasses the following anatomical structures, without limitation: lens, vitreous body, ciliary body, posterior chamber, anterior chamber, pupil, cornea, iris, canal of Schlemm, zonules of Zinn, limbus, conjunctiva, choroid, retina, central vessels of the retina, optic nerve, fovea centralis, macula lutea, and sclera.

"GPI 1605" refers a compound of formula



GPI 1605

"GPI 1046" refers to 3-(3-pyridyl)-1-propyl (2s)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidine-carboxylate, a compound of formula

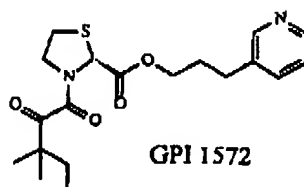


GPI 1046

38

In a preferred embodiment of the compounds of formula II, the heterocyclic ester or amide is the compound GPI 1572, of the formula

5



In a particularly preferred embodiment of formula  
10 II compounds:

A is CH<sub>2</sub>;

B is CH<sub>2</sub> or S;

C is CH<sub>2</sub> or NH;

R<sub>1</sub> is selected from the group consisting of 3-  
15 phenylpropyl and 3-(3-pyridyl)propyl; and

R<sub>2</sub> is selected from the group consisting of 1,1-dimethylpropyl, cyclohexyl, and tert-butyl.

Specific examples of this embodiment are presented in TABLE I.

20

**TABLE I**

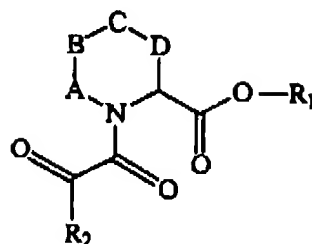
No.	A	B	C	R <sub>1</sub>	R <sub>2</sub>
1	CH <sub>2</sub>	S	CH <sub>2</sub>	3-phenylpropyl	1,1-dimethylpropyl
2	CH <sub>2</sub>	S	CH <sub>2</sub>	3-(3-pyridyl)propyl	1,1-dimethylpropyl
3	CH <sub>2</sub>	S	CH <sub>2</sub>	3-phenylpropyl	cyclohexyl
4	CH <sub>2</sub>	S	CH <sub>2</sub>	3-phenylpropyl	tert-butyl
5	CH <sub>2</sub>	CH <sub>2</sub>	NH	3-phenylpropyl	1,1-dimethylpropyl
6	CH <sub>2</sub>	CH <sub>2</sub>	NH	3-phenylpropyl	cyclohexyl
7	CH <sub>2</sub>	CH <sub>2</sub>	NH	3-phenylpropyl	tert-butyl

39

FORMULA III

The heterocyclic ester or amide may also be a compound of formula III

5



III

10

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B, C and D are independently CH<sub>2</sub>, O, S, SO, SO<sub>2</sub>, NH or NR<sub>1</sub>;

15

R<sub>1</sub> is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>5</sub> straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of (Ar<sub>1</sub>)<sub>n</sub> and C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl substituted with (Ar<sub>1</sub>)<sub>n</sub>;

20

n is 1 or 2;

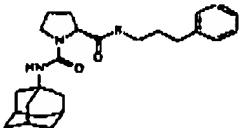
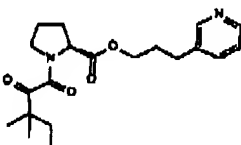
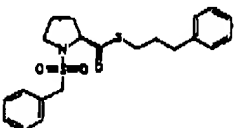
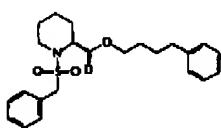
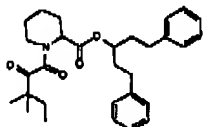
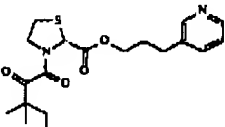
R<sub>2</sub> is either C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, or Ar<sub>1</sub>; and

25

Ar<sub>1</sub> is an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted with one

74

**Efficacy of representative compounds from  
different immunophilin ligand series  
in protecting retinal ganglion cell axons from  
degeneration following optic nerve transection**

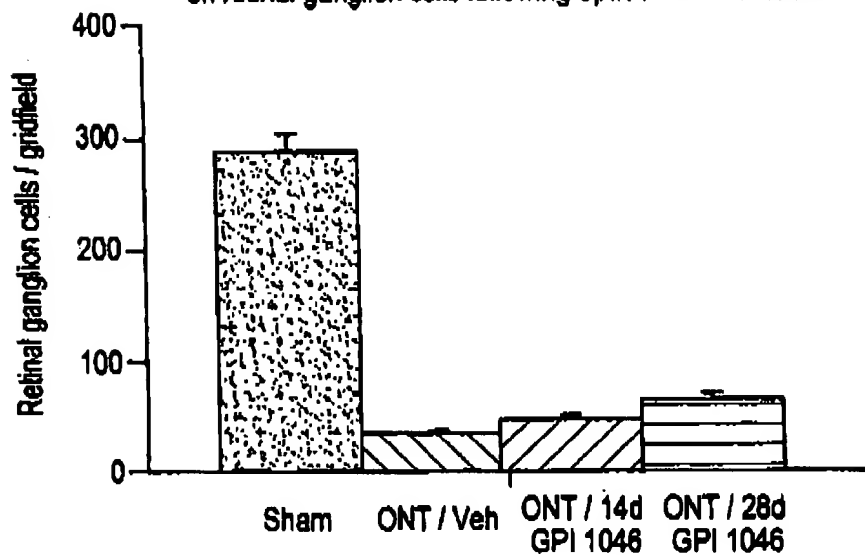
Compound	Structure	Comments	RT97+RGC axon density 14 days after ON transection (% ON axons rescued)
B		Adamantyl Thioester of urea Ki rotamase = 149 nM Clearance=? $\mu$ l/min	100.0% $\pm$ 5.2% SEM
A GPI 1046		Ester Ki rotamase = 7.5nM Clearance=63.8 $\mu$ l/min	60.5% $\pm$ 3.9 SEM
C		Sulfonamide Ki rotamase = 107nM Clearance= 31.1 $\mu$ l/min	60.4% $\pm$ 3.1 % SEM
D		Pipecolic sulfonamide Ki rotamase= nM Clearance= $\mu$ l/min	58.4% $\pm$ 6.4% SEM
E		Ester of pipecolic acid Ki rotamase = 20 nM Clearance = 41.8 $\mu$ l/min	56.6% $\pm$ 9.4% SEM
F		Proline heterocycle Analog of GPI 1046 Ki rotamase = 272 nM Clearance=? $\mu$ l/min	55.1% $\pm$ 5.9% SEM

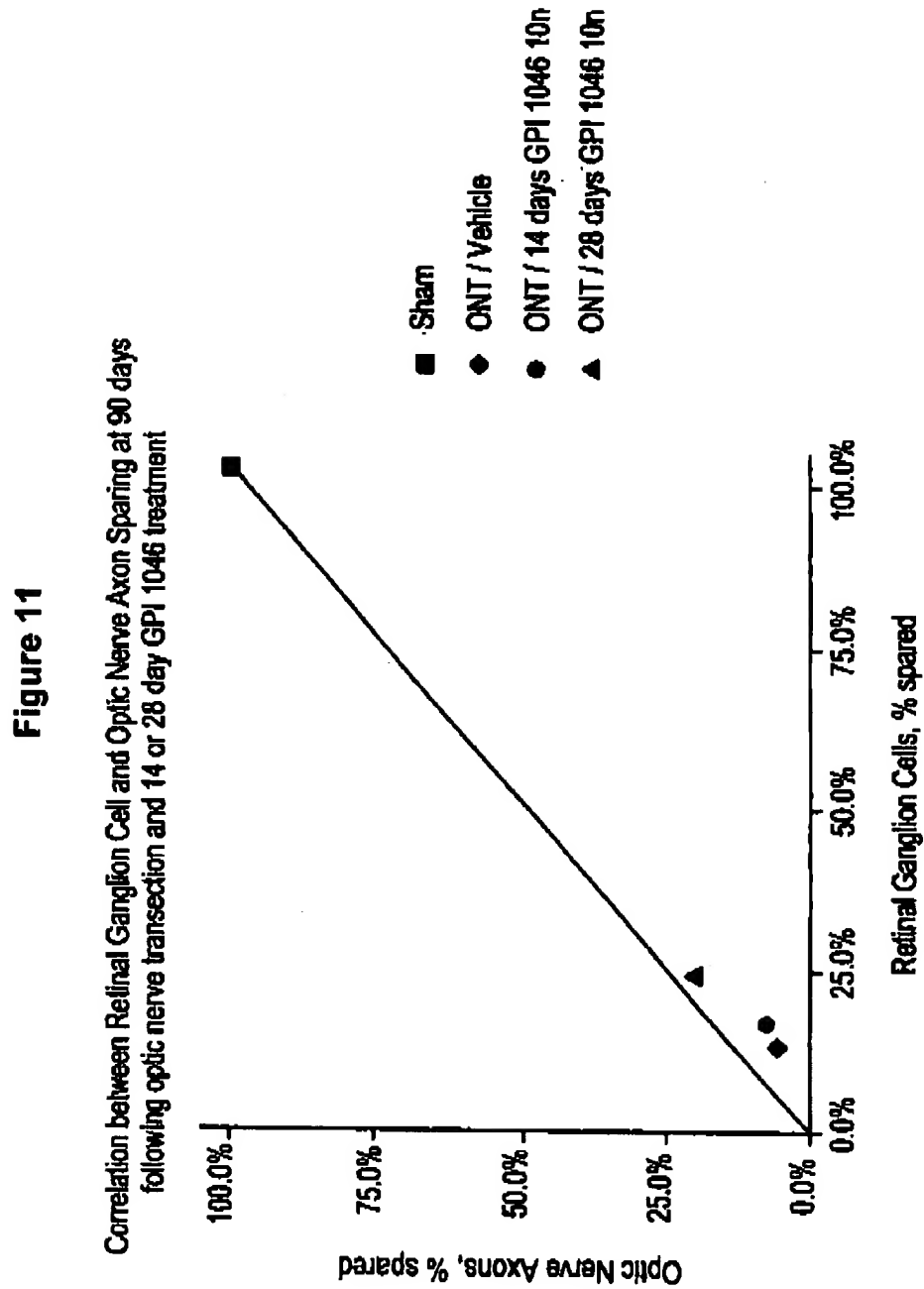
**TABLE V**

Appl. No. 09/134,419  
NEW SHEET

**Figure 10**

Neuroprotective effect of GPI 1046  
on retinal ganglion cells following optic nerve transection



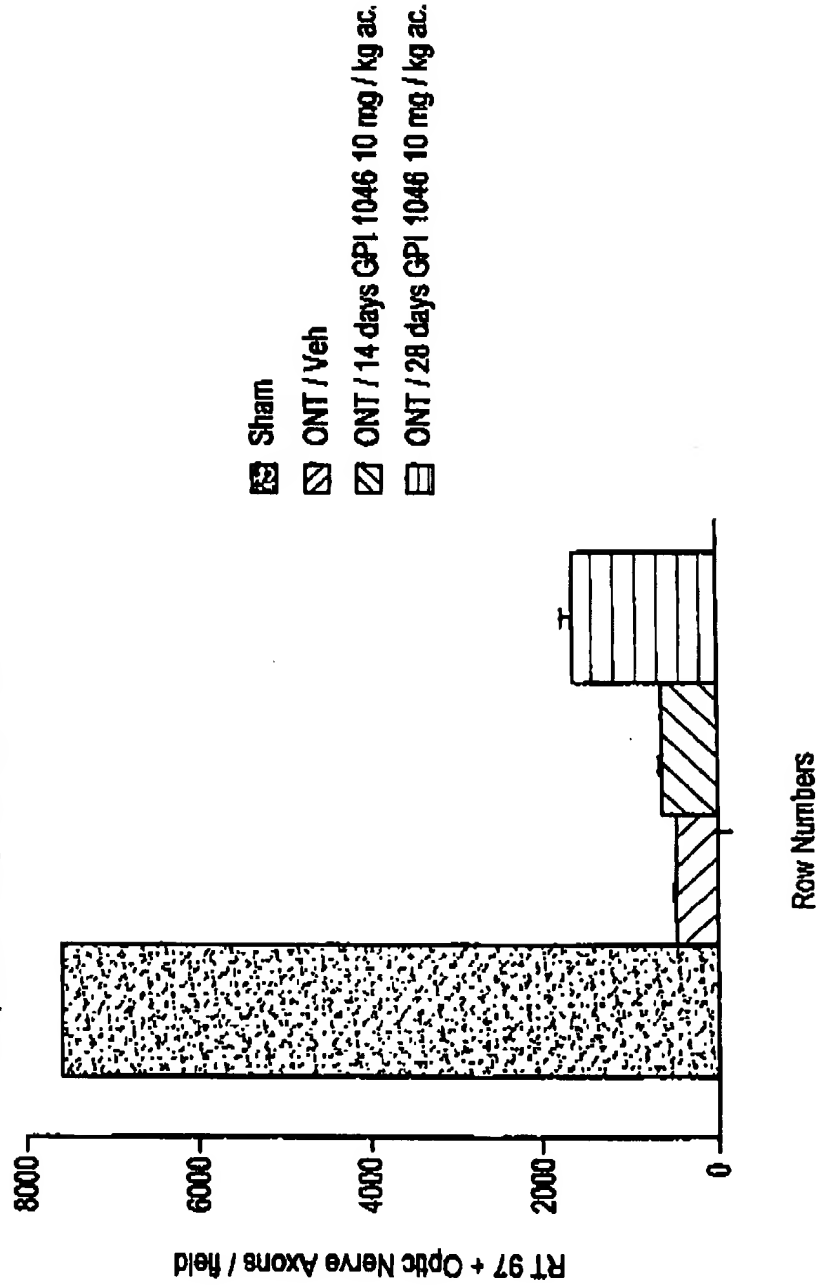
Appl. No. 09/134,419  
NEW SHEET



Appl. No. 09/134,419  
NEW SHEET

**Figure 12**

GPI 1046 preserves optic nerve axons  
in the proximal stump following transection



Atty. Dkt. No. 087579-0857

## REMARKS

Entry of the foregoing amendment is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 25-OCT-2007

By 

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 295-4059  
Facsimile: (202) 672-5399

Rouget F. Henschel  
Attorney for Applicant  
Registration No. 39,221